UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,998	06/14/2001	Maria Adele Pacciarini	01-270	1122

20306 7590 09/09/2003

MCDONNELL BOEHNEN HULBERT & BERGHOFF
300 SOUTH WACKER DRIVE
SUITE 3200
CHICAGO, IL 60606

EXAMINER	
OWENS JR, HOWARD V	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,998	PACCIARINI ET AL.	
	Examiner	Art Unit	
	Howard V Owens	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,14 and 18-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14 and 18-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Arguments

The following is in response to the amendment filed 4/09/03:

An action on the merits of claims 13, 14, 18-31 is contained herein below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 U.S.C. § 103

Applicant's arguments filed 4/9/03 have been fully considered but they are not persuasive. The rejection of claims 13, 14, 18, 19 and 20-31(newly added) are rejected under 35 U.S.C. § 103 as being unpatentable over Kuhl et al., Cancer Chemotherap. Pharmacol., 33(1), pp. 10-16 (abstract) in combination with Miura et al., Gan To Kagaku Ryoho 25(9), 1262-5 (English abstract) and newly added Gorbunova, Intrahepatic Arterial Infusion Chemotherapy for Primary and Metastatic Cancer of the Liver.

Claims 13 and 14 are drawn to a pharmaceutical composition which comprises MMDX and a pharmaceutically acceptable agent, iodized oil, which remains selectively in a liver tumor after its injection through the hepatic artery.

Claim 18 is drawn to a method for treating a human liver tumor which comprises intrahepatic administration of a therapeutically effective amount of MMDX to a patient in need thereof. Dependent claims 20-31 are drawn to intrahepatic artery administration of MMDX.

Claim 19 is drawn to a method for reducing systemic exposure of a patient suffering from a liver cancer which comprises the intrahepatic administration of a therapeutically effective amount of MMDX to said patient.

Miura et al. teach the treatment of liver tumors or hapatocellular carcinomas of via hepatic artery administraton of doxorubicin and lipiodol (iodized oil) to decrease tumor volume or cause remission. However it does not teach the use of MMDX, a doxorubicin analog, via hepatic artery administration.

Kuhl teaches that MMDX as a doxorubicin analog, not only has the same tumor specificity as doxorubicin, it is activated in the liver to a metabolite whose potency is 10

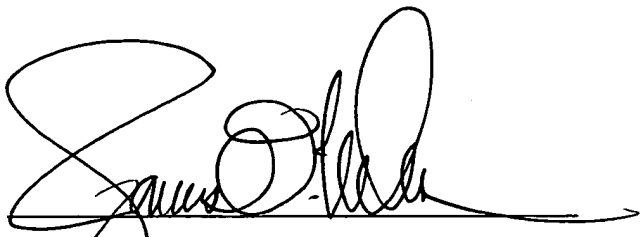
times greater and Gorbunova provides the nexus for intrahepatic arterial infusion as it teaches that IHAIC creates super high concentrations of an antitumor agent in the organ affected, which adequately bridges the nexus between the prior art and the invention as claimed.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to administer MMDX via the hepatic artery.

A person of ordinary skill in the art would have been motivated to use MMDX in hepatic artery administration since the prior art recognizes that hepatic artery administration of doxorubicin is beneficial for decreasing tumor volume within hepatic carcinomas and reducing systemic exposure via direct administration to the organ; moreover, one of skill in the art would have a reasonable expectation of success in the use of a more potent analog of doxorubicin, MMDX, in the same method of treatment.

Applicant's primary argument is that intrahepatic arterial administration of MMDX is not taught; however, as cited supra, for the combination of MMDX with iodized oil, Miura et al. teach the treatment of liver tumors or hapatocellular carcinomas of via hepatic artery administraton of doxorubicin (of which MMDX is an analog) and lipiodol (iodized oil) to decrease tumor volume or cause remission. For lone use of MMDX, Gorbunova teaches that intrahepatic arterial administration of a chemotherapeutic creates super high concentrations in the organ affected, this localization of treatment is clearly beneficial for reducing systemic exposure. Applicant's assertion that MMDX as an analog could not be expected to behave like doxorubicin is also not persuasive. Applicant's assertions do not serve as fact and applicant has produced no evidence that the analog MMDX is so varied in it's structure, effect and target that one of skill in the art would not have a reasonable expectation of success. MMDX is not just a member of the class of anthracyclines, it is an analog of doxorubicin, and as cited supra, Kuhl teaches that "MMDX as a doxorubicin analog, not only has the same tumor specificity as doxorubicin, it is activated in the liver to a metabolite whose potency is 10 times greater". Given that doxorubicin and MMDX are analogs of one another with the same tumor specificity, in the absence of evidence to the contrary, applicant's assertions regarding the prior art and the expectation of one of skill in the art are not convincing.

Howard V. Owens
Patent Examiner
Art Unit 1623



James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538 . The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner signing this action, James O. Wilson can be reached on (703) 308-4624 . The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.